WASHINGTON UNIVERSITY

SCHOOL OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE
BARNES AND WOHL HOSPITALS
600 SOUTH KINGSHIGHWAY
ST. LOUIS 10, MISSOURI

12 April 1961

Dr. Joshua Lederberg
Department of Genetics
Stanford University Medical School
Palo Alto, California

Dear Josh:

Kern, Helmreich and I have revised the enclosed manuscript so as to comply with most of the objections raised by you and Mel Cohn. The major difficulty we encountered was the matter of whether or not microsomal antibodies are attached to ribosomes or to other components of the microsomal fraction; e.g., endoplasmic reticulum. The previous experience here was that deoxycholate treatment was ambiguous in that most of the antibody activity was removed from the ribosomes but some definitely adhered. Since deoxycholate can obviously do much more than simply separate the two principle microsomal components we clearly had no confidence in interpretation of these results. But the deep reservations we had were not, I see now, expressed clearly enough so that one can now see where Mel's difficulty occurred. Since having the manuscript returned Milt has repeated the experiments with deoxycholate and obtained similar results to his previous ones: i.e., nearly all of the microsomal antibody activity is removed from the particles. Moreover when the residual small amount of activity is normalized for ribosomal protein or RNA or the sum of these two, it is clear that the antibody activity remaining on the ribosomes is tremendously reduced in amount relative to the parental microsomal fraction. In part the magnitude of this depletion effect of deoxycholate seems greater to us now than it did before because we now use the correct extinction coefficient for ribosomal protein which is surprisingly low ($E|^{1\%}_{1cm}=7$). All of this provides no answer of course as to where antibodies attached in the microsomal fraction and the corresponding segment of the manuscript has been re-written so as to make clear as possible that we have no answer now to this question.

I do not know that we can do any more and look forward to hearing what your reaction is to the manuscript in its present form. With best wishes,

Sincerely yours,

Herman N. Eisen

Herman N. Eisen

HNE:vb
enc.